Table 2. Genetic Alterations sensitizing mammalian cells to Top1 poisons

Genes	Functions	Refs.
APTX	Mutated in AOA1; Encodes aprataxin, which associate XRCC1 (Fig. 5B)	(*210*)
ATM [a]	Mutated in AT; Protein kinase from the PI3K family implicated in DSB response	(*211-214*)
ATR	Protein kinase from the PI3K family; Implicated in replication stress	(*163*)
BCL-2	Mutated in B-cell lymphoma; Apoptosis	(*215*)
BLM	Mutated in BS; Helicase from the RecQ family involved in genomic stability	(*79, 82*)
BRCA1	Mutated in familial breast cancers; DNA damage response; TC-NER	(*216*)
BRCA2	Mutated in familial breast cancers; Rad51 loading; Homologous recombination	(*217*)
CSA/CSB	Mutated in CS; TCR/BER	(*76*)
Chk1	Checkpoint kinase phosphorylated/activated by PI3K (ATR)	(*162, 165*)
Chk2	Checkpoint kinase phosphorylated/activated by PI3K (ATM etc…)	(*162, 218*)
DNA-PKcs	Protein kinase from the PI3K family; Implicated in DSB response	(*56, 219, 220*)
FEN-1	Flap and gap endonuclease; processing of stalled replication forks	(*133*)
H2AX	Core histone; phosphorylated in response to DSB (γ-H2AX foci)	(*53*)
NBS1	Mutated in NBS; Scaffolding protein forming a complex with Mre11 and Rad50 (MRN complex); DSB repair and recombination pathways	(*212, 221*)
PARP	BER (see Fig. 7)	(*118, 222*)
PNKP/hPNK	Processing of DNA ends: 3'-DNA-phosphatase + 5'-DNA-kinase	(*115*)
Rad51C	One of the five Rad51 paralogs; Implicated in DNA strand exchange/homologous recombination	(*223*)
TDP1	Mutated in SCAN; Hydrolysis of 3'-phosphodiesters (phosphotyrosyl and phosphoglycolate) and phosphamides (Tdp1 cleavage complex)	(*93, 94, 224*)
TP53	Mutated in Li-Fraumeni syndrome; encodes p53; Checkpoints; apoptosis	(*225, 226*)
WRN	Mutated in Werner syndrome; RecQ helicase involved in genomic stability	(*227-229*)
XRCC1	BER; binds to Tdp1, PARP, β-polymerase, ligase III and aprataxin	(*116, 117, 119, 230-233*)
XRCC2	One of the five Rad51 paralogs: Rad51B, Rad51C, Rad51D, XRCC2 & XRCC3; Implicated in DNA strand exchange/homologous recombination	(*219, 230, 234*)
XRCC3	One of the five Rad51 paralogs; Implicated in DNA strand exchange/homologous recombination	(*167, 219*)

[a] The contribution of ATM has not been found consistently: ATM-siRNA cells are not hypersensitive to camptothecin (*162*) and we found that AT-complemented cells are not hypersensitive to camptothecin (our unpublished results).

Genes are in alphabetic order.

Abbreviations: AOA1: Ataxia-oculomotor apraxia 1; ATM: Ataxia Telangiectasia Mutant; ATR: Ataxia Telangiectasia and Rad3-related; BER: Base Excision Repair; BLM: Bloom syndrome (BS); CSA/CSB: Cockayne Syndrome (CS) complementation groups A and B; DNA-PKcs: DNA-dependent protein kinase catalytic subunit; DSB: DNA double-strand breaks; NBS: Nijmegen Breakage Syndrome; NER: nucleotide excision repair; PARP: poly(ADP-ribose) polymerase; PI3K: phosphatidyl inositol 3 kinase; PNKP: polynucleotide kinase phosphatase; SCAN: Spino Cerebellar Ataxia Axonal Neuropathy; TCR: transcription-coupled repair; WRN: Werner syndrome.